

## Alternative Test Method Project Milestones

This page provides a current summary of the status of ongoing and completed NICEATM-ICCVAM alternative test method evaluation projects, as well as projects to which NICEATM, ICCVAM, and agency scientists are contributing.

### Alternative test methods:

- Reduce the number of animals used to the minimum number required to obtain scientifically valid data
- Refine procedures to lessen or eliminate animal pain and distress
- Replace animals with non-animal systems or one animal species with a less highly developed one (for example, replacing a mouse with a fish)

### *Acute Oral Systemic Toxicity Projects*

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Up-and-Down Procedure (oral)	√	√	√	√	2002	2002 (OECD TG 425)
Fixed Dose Procedure (oral)	√	√	√	√	2002	2002 (OECD TG 420)
Acute Toxic Class Method (oral)	√	√	√	√	2002	2002 (OECD TG 423)
<i>In Vitro</i> Cytotoxicity Test Methods: 3T3 cells	√	√	√	√	2008	2010 (OECD GD 129)
<i>In Vitro</i> Cytotoxicity Test Methods: NHK cells	√	√	√	√	2008	2010 (OECD GD 129)

### *Acute Inhalation Systemic Toxicity Projects*

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Acute Toxic Class Method (inhalation)	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2009 (OECD TG 436)
Fixed Dose Procedure (inhalation)	√	√	<i>Anticipated 2010 (OECD)</i>	<i>(Not applicable – to be adopted via OECD Test Guideline)</i>		<i>Anticipated 2010 (OECD)</i>

### *Acute Dermal Systemic Toxicity Projects*

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Up-and-Down Procedure (dermal)	√	<i>In progress: Anticipated 2010</i>	<i>Anticipated 2011</i>	<i>Anticipated 2011</i>	<i>Anticipated 2012</i>	

### ***In Vitro Metabolism and Toxicokinetics Projects***

<b>Test Method</b>	<b>R&amp;D</b>	<b>Validation</b>	<b>Evaluation</b>	<b>Recommendations to U.S. Agencies</b>	<b>U.S. Acceptance</b>	<b>International Acceptance</b>
Provision of a Standard for Human Hepatic Metabolism and Toxicity by Assessing as an Indicator Biotransformation Enzyme Induction Using HepaRG® Cells and Cryopreserved Human Hepatocytes	√	<i>In progress: Anticipated 2011</i>	<i>Anticipated 2011 (OECD)</i>	<i>(Not applicable – to be adopted via OECD Test Guideline)</i>		<i>Anticipated 2012 (OECD)</i>

### ***Dermal Corrosivity Projects***

<b>Test Method</b>	<b>R&amp;D</b>	<b>Validation</b>	<b>Evaluation</b>	<b>Recommendations to U.S. Agencies</b>	<b>U.S. Acceptance</b>	<b>International Acceptance</b>
Corrositex® Assay	√	√	√	√	2000	2006 (OECD TG 435)
EpiDerm™ Assay	√	√	√	√	2004	2004 (OECD TG 431)
EPISKIN™ Assay	√	√	√	√	2004	2004 (OECD TG 431)
Rat Transcutaneous Electrical Resistance Assay	√	√	√	√	2004	2004 (OECD TG 430)
SkinEthic RHE Assay	√	√	√	√	2004	2004 (OECD TG 431)
LabCyte EPI-MODEL24 Assay	√	√	<i>In progress: Anticipated 2010 (OECD)</i>			

### ***Dermal Irritation Projects***

<b>Test Method</b>	<b>R&amp;D</b>	<b>Validation</b>	<b>Evaluation</b>	<b>Recommendations to U.S. Agencies</b>	<b>U.S. Acceptance</b>	<b>International Acceptance</b>
EpiDerm™ Assay	√	√	<i>In progress: (OECD) Anticipated 2010</i>			
EPISKIN™ Assay	√	√	<i>In progress: (OECD) Anticipated 2010</i>			
SkinEthic RHE Assay	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2010 (OECD TG 439)
LabCyte EPI-MODEL24 Assay	√	√	<i>In progress: (OECD) Anticipated 2010</i>			

### ***Ocular Toxicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Bovine Corneal Opacity and Permeability (BCOP) - Ocular Corrosivity/Severe Irritation	√	√	√	√	2008	2009 (OECD TG 437)
Isolated Chicken Eye (ICE) - Ocular Corrosivity/Severe Irritation	√	√	√	√	2008	2009 (OECD TG 438)
Hen's Egg Test/Chorioallantoic Membrane (HET-CAM) - Ocular Corrosivity/Severe Irritation	√	√	√	ICCVAM review in 2007 found that this test method was not sufficiently accurate for regulatory use and recommended additional studies		
Isolated Rabbit Eye (IRE) - Ocular Corrosivity/Severe Irritation	√	√	√	ICCVAM review in 2007 found that this test method was not sufficiently accurate for regulatory use and recommended additional studies		
Integrated Non-animal Testing Strategy for Eye Irritation Potential of Antimicrobial Cleaning Products	√	√	√	√	Anticipated 2011	
BCOP - Nonsevere Ocular Irritation	√	√	√	√	Anticipated 2011	
HET-CAM - Nonsevere Ocular Irritation	√	√	√	√	Anticipated 2011	
ICE - Nonsevere Ocular Irritation	√	√	√	√	Anticipated 2011	
IRE - Nonsevere Ocular Irritation	√	√	√	√	Anticipated 2011	
Cytosensor Microphysiometer Test Method	√	√	√	√	Anticipated 2011	
Routine use of topical anesthetics, systemic analgesics and humane endpoints in <i>in vivo</i> testing	√	√	√	√	Anticipated 2011	
The <i>In Vivo</i> Low Volume Eye Test	√	√	√	√	-	
Fluorescein Leakage Test Method - Nonsevere Ocular Irritation	√	√	√	ICCVAM reviewed in 2009; however, because the validation study data were not publicly available, ICCVAM recommendations were not made		
Neutral Red Release Test Method - Nonsevere Ocular Irritation	√	√	ICCVAM review in 2009 found that this test method was not adequately validated for regulatory use			
Red Blood Cell Haemolysis Test Method - Nonsevere Ocular Irritation	√	√	ICCVAM review in 2008 found that this test method was not adequately validated for regulatory use			

### ***Immunotoxicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Murine Local Lymph Node Assay (LLNA)	√	√	√	√	1999	2002 (OECD TG 429)
Updated LLNA protocol (20% animal reduction)	√	√	√	√	2010	2010 (Updated OECD TG 429)
Reduced LLNA Test Method	√	√	√	√	2010	2010 (Updated OECD TG 429)
Development of LLNA Performance Standards	√	√	√	√	2010	2010 (Updated OECD TG 429)
Non-radiolabeled LLNA method: LLNA:DA	√	√	√	√	<i>Anticipated 2010</i>	2010 (OECD TG 442A)
Non-radiolabeled LLNA method: LLNA:BrdU-ELISA	√	√	√	√	<i>Anticipated 2010</i>	2010 (OECD TG 442B)
Non-radiolabeled LLNA method: LLNA: BrdU-Flow Cytometry	√	<i>Inter-laboratory validation study required</i>				
Use of the LLNA for Testing Pesticide Formulations, Metals, and Aqueous Solutions	√	√	√	√	<i>Anticipated 2010</i>	2010 (Updated OECD TG 429)
Use of the LLNA for Skin Sensitization Potency Categorization	√	√	<i>Anticipated 2010</i>	<i>Anticipated 2010</i>	<i>Anticipated 2011</i>	

### ***Dermal Phototoxicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
3T3 NRU Phototoxicity Test	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2004 (OECD TG 432)
3T3 NRU Phototoxicity Test: Application to UV Filter Chemicals	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2004 (OECD TG 432)

### ***Dermal Absorption Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
<i>In Vitro</i> Dermal Absorption	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2004 (OECD TG 428)

### ***Genetic Toxicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
<i>In Vitro</i> Micronucleus Assay	√	√	√	(Not applicable – adopted via OECD Test Guideline)		2010 (OECD TG 487)
<i>In vivo</i> comet assay	√	<i>In progress</i>				
<i>In vitro</i> comet assay	√	<i>In progress</i>				
Cell transformation assays	√	√	<i>In progress</i>			
BHAS cell transformation assay	√	<i>In progress</i>				

### ***Developmental Toxicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
Frog Embryo Teratogenesis Assay: Xenopus (FETAX)	√	√	√	ICCVAM review in 2000 found that FETAX was not sufficiently reliable for regulatory use and provided recommendations for improving accuracy and reliability		

### ***Endocrine Disruptor Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
<i>In vitro</i> Androgen Receptor (AR) Binding	√	ICCVAM review in 2004 found validation studies conducted to date to be inadequate - ICCVAM published recommendations on future validation studies				
<i>In vitro</i> AR Transcriptional Activation (TA)	√	ICCVAM review in 2004 found validation studies conducted to date to be inadequate - ICCVAM published recommendations on future validation studies				
<i>In vitro</i> Estrogen Receptor (ER) Binding	√	ICCVAM review in 2004 found validation studies conducted to date to be inadequate - ICCVAM published recommendations on future validation studies				
<i>In vitro</i> ER TA	√	ICCVAM review in 2004 found validation studies conducted to date to be inadequate - ICCVAM published recommendations on future validation studies				
LUMICELL® ER TA Assay Evaluation	√	√	<i>Anticipated 2011</i>	<i>Anticipated 2011</i>	<i>Anticipated 2011</i>	
MCF-7 Cell Proliferation Assay Evaluation	√	<i>In progress: Anticipated 2010</i>	<i>Anticipated 2011</i>	<i>Anticipated 2011</i>	<i>Anticipated 2011</i>	

### ***Pyrogenicity Projects***

Test Method	R&D	Validation	Evaluation	Recommendations to U.S. Agencies	U.S. Acceptance	International Acceptance
The Human Whole Blood/IL-1 <i>In Vitro</i> Pyrogen Test	√	√	√	√	2009	
The Human Whole Blood/IL-1 <i>In Vitro</i> Pyrogen Test Using Cryopreserved Human Whole Blood	√	√	√	√	2009	
The Human Whole Blood/IL-6 <i>In Vitro</i> Pyrogen Test (WB/IL-6)	√	√	√	√	2009	
<i>In Vitro</i> Pyrogen Test Using Human Peripheral Blood Mononuclear Cells (PBMC/IL-6)	√	√	√	√	2009	
An Alternative <i>In Vitro</i> Pyrogen Test Using the Human Monocytoid Cell Line MONO MAC 6 (MM6/IL-6)	√	√	√	√	2009	

### ***Biologics and Vaccines Projects***

<b>Test Method</b>	<b>R&amp;D</b>	<b>Validation</b>	<b>Evaluation</b>	<b>Recommendations to U.S. Agencies</b>	<b>U.S. Acceptance</b>	<b>International Acceptance</b>
Humane Endpoints in Animal Testing of Biological Products	√	√	√	√	2004	
Humane Endpoints in Animal Testing of Rabies Vaccines	√	√	√	√	2004	
<i>In Vivo</i> Refinement Alternatives for Botulinum Toxin Potency Testing	√	ICCVAM workshop in 2006 assessed the state of the science and concluded that additional development and validation of these methods were needed prior to evaluation by ICCVAM.				
<i>Ex Vivo</i> Alternatives for Botulinum Toxin Potency Testing	√	ICCVAM workshop in 2006 assessed the state of the science and concluded that additional development and validation of these methods were needed prior to evaluation by ICCVAM.				
Cell-based Alternatives for Botulinum Toxin Potency Testing	√	ICCVAM workshop in 2006 assessed the state of the science and concluded that additional development and validation of these methods were needed prior to evaluation by ICCVAM.				
Endopeptidase Assay Alternatives for Botulinum Toxin Potency Testing	√	ICCVAM workshop in 2006 assessed the state of the science and concluded that additional development and validation of these methods were needed prior to evaluation by ICCVAM.				
Alternative Methods for Vaccine Potency and Safety Testing	√	<i>An ICCVAM workshop in September 2010 assessed the state of the science and identified priorities for research, development, and validation efforts; report detailing conclusions and recommendations to be published in 2011.</i>				

***Acute Oral Systemic Toxicity  
Up-And-Down Procedure***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. The Up-And-Down Procedure reduces animal use for this purpose by up to 70%.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Publication of OECD Test Guideline 425	1998	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg425.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg425.pdf</a>
Nomination by the U.S. Environmental Protection Agency (EPA)	August 1999	-
Peer Review Panel Meeting	July 2000	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/udp_report.htm">http://iccvam.niehs.nih.gov/methods/acutetox/udp_report.htm</a>
Peer Review Panel Follow-up Teleconference	August 2001	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/udp_report.htm">http://iccvam.niehs.nih.gov/methods/acutetox/udp_report.htm</a>
Test Method Evaluation Report Published	November 2001	Vol 1: <a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/udpProc/udpfin01/vol_1.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/udpProc/udpfin01/vol_1.pdf</a> Vol 2: <a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/udpProc/udpfin01/vol_2.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/udpProc/udpfin01/vol_2.pdf</a>
Recommendations Made to Federal Agencies	March 2003	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/udp.htm">http://iccvam.niehs.nih.gov/methods/acutetox/udp.htm</a>
Federal Agency Responses Received	December 2003	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/udp.htm">http://iccvam.niehs.nih.gov/methods/acutetox/udp.htm</a>

***Fixed Dose Procedure (oral)***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. The Fixed Dose Procedure reduces animal use for this purpose by up to 70%.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Publication of OECD Test Guideline 420	1998	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD_GL420.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD_GL420.pdf</a>

***Acute Toxic Class Method (oral)***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. The Fixed Dose Procedure reduces animal use for this purpose by up to 70%.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Publication of OECD Test Guideline 423	1998	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD_GL423.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD_GL423.pdf</a>

### ***Evaluation of In Vitro Cytotoxicity Test Methods***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. <i>In Vitro</i> Cytotoxicity Test Methods replace animal use for initial dose setting for these tests.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
EPA Nomination	August 1999	-
Workshop Held	October 2000	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/invidocs/IV_doc.htm">http://iccvam.niehs.nih.gov/methods/acutetox/invidocs/IV_doc.htm</a>
Guidance Document Published	August 2001	<a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/guidance0801/iv_guide.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/guidance0801/iv_guide.pdf</a>
Workshop Report Published	August 2001	<a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/finalrpt/finalall0801.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/finalrpt/finalall0801.pdf</a>
Recommendations Made to Federal Agencies	March 2003	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_cyto.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_cyto.htm</a>
Federal Agency Responses Received	December 2003	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_cyto.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_cyto.htm</a>

### ***Validation Study of In Vitro Cytotoxicity Test Methods***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. Neutral Red Uptake Test Methods replace animal use for initial dose setting for these tests.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Peer Review Panel Meeting	May 2006	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_scepeerrev.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_scepeerrev.htm</a>
Peer Review Panel Report Published	June 2006	<a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/ATpanelrpt06/ATpanelrpt.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/ATpanelrpt06/ATpanelrpt.pdf</a>
Background Review Document Published	November 2006	Vol 1: <a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/BRD_TMER/BRDvol1_Nov2006.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/BRD_TMER/BRDvol1_Nov2006.pdf</a> Vol 2: <a href="http://iccvam.niehs.nih.gov/docs/acutetox_docs/BRD_TMER/BRDvol2_Nov2006.pdf">http://iccvam.niehs.nih.gov/docs/acutetox_docs/BRD_TMER/BRDvol2_Nov2006.pdf</a>
Test Method Evaluation Report Published	November 2006	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_tmter.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_tmter.htm</a>
Recommendations Made to Federal Agencies	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_recommend.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_recommend.htm</a>
Federal Agency Responses Received	September 2008	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_recommend.htm">http://iccvam.niehs.nih.gov/methods/acutetox/inv_nru_recommend.htm</a>
OECD Guidance Document 129 Published	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-GD129.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-GD129.pdf</a>



### ***Developing and Advancing In Vitro Alternatives to Acute Chemical Systemic Toxicity Testing***

Acute oral systemic toxicity testing identifies substances that are poisonous when ingested so that they may be appropriately labeled and packaged. An ICCVAM-sponsored workshop explored ways to reduce, refine, or replace animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Workshop Held	February 2008	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/Tox_workshop.htm">http://iccvam.niehs.nih.gov/methods/acutetox/Tox_workshop.htm</a>
Workshop Report Published	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/acutetox/toxwksp-rpt.htm">http://iccvam.niehs.nih.gov/methods/acutetox/toxwksp-rpt.htm</a>

### ***Acute Inhalation Toxicity***

#### ***Acute Toxic Class Method***

Acute inhalation systemic toxicity testing identifies substances that are poisonous when inhaled so that they may be appropriately labeled and packaged. The Acute Toxic Class Method reduces animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Publication of Test Guideline 436	September 2009	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG436.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG436.pdf</a>

### ***Dermal Corrosivity***

#### ***Evaluation of Corrositex® for the Identification of Substances Potentially Corrosive to Human Skin***

Dermal corrosivity testing identifies substances that cause chemical burns to the skin so that they may be appropriately labeled and packaged. Corrositex® reduces and refines animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Corrositex® Submission	May 1998	-
Peer Review Panel Meeting	January 1999	<a href="http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm">http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm</a>
Peer Review Panel Report Published	June 1999	<a href="http://iccvam.niehs.nih.gov/docs/reports/corprrep.pdf">http://iccvam.niehs.nih.gov/docs/reports/corprrep.pdf</a>
Recommendations Made to Federal Agencies	June 1999	<a href="http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm">http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm</a>
Federal Agency Responses Received	October 1999	<a href="http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm">http://iccvam.niehs.nih.gov/methods/dermal/corrode.htm</a>
Publication of OECD Test Guideline 435	July 2006	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg435.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg435.pdf</a>

***Evaluation of EpiSkin™, EPIDERM™ and the Rat Skin Transcutaneous Electrical Resistance Assay (TER) for the Identification of Substances Potentially Corrosive to Human Skin***

Dermal corrosivity testing identifies substances that cause chemical burns to the skin so that they may be appropriately labeled and packaged. Use of these <i>in vitro</i> tests reduces and refines animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Background Review Document Published	August 2001	<a href="http://iccvam.niehs.nih.gov/docs/dermal_docs/epis_brd0801.pdf">http://iccvam.niehs.nih.gov/docs/dermal_docs/epis_brd0801.pdf</a>
Test Method Evaluation Report Published	June 2002	<a href="http://iccvam.niehs.nih.gov/docs/dermal_docs/cwgfinal02/cwgfinal0602.htm">http://iccvam.niehs.nih.gov/docs/dermal_docs/cwgfinal02/cwgfinal0602.htm</a>
Recommended Performance Standards Published	May 2004	<a href="http://iccvam.niehs.nih.gov/methods/dermal/epiderm/ps/ps044510.pdf">http://iccvam.niehs.nih.gov/methods/dermal/epiderm/ps/ps044510.pdf</a>
Publication of OECD Test Guidelines 430 and 431	July 2006	TG 430 – <a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg430.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg430.pdf</a> TG 431 - <a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg431.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg431.pdf</a>
Updates Submitted to OECD Test Guidelines 430 and 431	July 2009	-

***Dermal Irritation***

***Evaluation of EpiSkin™, EPIDERM™ and the SkinEthic RHE Assay for the Identification of Substances Potentially Irritating to Human Skin***

Dermal irritation testing identifies substances that cause irritation to the skin so that they may be appropriately labeled and packaged. Use of these <i>in vitro</i> tests reduces animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Submission of ICCVAM Comments on Draft Test Guideline to U.S. OECD National Coordinator	August 2008	<a href="http://iccvam.niehs.nih.gov/methods/dermal/dermal-oecd.htm">http://iccvam.niehs.nih.gov/methods/dermal/dermal-oecd.htm</a>
OECD Expert Meeting	June 2009	-
Publication of OECD Test Guideline 439	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG439.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG439.pdf</a>

***Ocular Toxicity***

***In Vitro Test Methods for Detecting Ocular Corrosives and Severe Irritants***

- Bovine Corneal Opacity and Permeability Test Method
- Isolated Chicken Eye Test Method
- Isolated Rabbit Eye Test Method
- Hen's Egg Test - Chorioallantoic Membrane Test Method

Ocular toxicity testing identifies substances that may cause permanent or temporary blindness. Use of these <i>in vitro</i> test methods will reduce and refine animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
EPA Nomination	October 2003	-
Expert Panel Meeting	January 2005	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_report.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_report.htm</a>
Expert Panel Report	March 2005	<a href="http://iccvam.niehs.nih.gov/docs/ocutox_docs/EPreport/ocuEPrt.pdf">http://iccvam.niehs.nih.gov/docs/ocutox_docs/EPreport/ocuEPrt.pdf</a>
Expert Panel Teleconference	September 2005	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_report.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_report.htm</a>

Expert Panel Report Addendum	November 2005	<a href="http://iccvam.niehs.nih.gov/docs/ocutox_docs/EPreport/addendum/EPrptAddend.pdf">http://iccvam.niehs.nih.gov/docs/ocutox_docs/EPreport/addendum/EPrptAddend.pdf</a>
Background Review Documents Published	October 2007	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_bckgnd.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_bckgnd.htm</a>
Test Method Evaluation Report Published	October 2007	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_TMER.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_TMER.htm</a>
Recommendations Made to Federal Agencies	October 2007	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_recommen d.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_recommen d.htm</a>
Federal Agency Responses Received	May 2008	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_recommen d.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/ocu_recommen d.htm</a>
Draft OECD Test Guidelines 437 (BCOP) and 438 (ICE) Submitted to U.S. National Coordinator	August 2008	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/OECD.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/OECD.htm</a>
Adoption of OECD Test Guidelines	September 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/OECD.htm">http://iccvam.niehs.nih.gov/methods/ocutox/ivocutox/OECD.htm</a>

### ***Routine Use of Topical Anesthetics, Systemic Analgesics, and Humane Endpoints In In Vivo Testing***

Ocular toxicity testing identifies substances that may cause irritation to the eye. Routine use of topical anesthetics, systemic analgesics, and humane endpoints in <i>in vivo</i> testing will refine animal use for this purpose by eliminating or reducing animal pain and distress.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Peer Review Panel Meeting	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Peer Review Panel Report Published	July 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Recommendations Made to Federal Agencies	September 2010	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/pretreat.htm">http://iccvam.niehs.nih.gov/methods/ocutox/pretreat.htm</a>

### ***In Vitro Test Methods for Detecting Nonsevere Ocular Irritants***

- Bovine Corneal Opacity and Permeability Test Method
- Isolated Chicken Eye Test Method
- Cytosensor Microphysiometer Test Method
- Isolated Rabbit Eye Test Method
- Hen's Egg Test - Chorioallantoic Membrane Test Method

Ocular toxicity testing identifies substances that may cause irritation to the eye. Use of these <i>In Vitro</i> Test Methods will reduce and refine animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
EPA Nomination	October 2003	-
Peer Review Panel Meeting	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Peer Review Panel Report Published	July 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Recommendations Made to Federal Agencies	September 2010	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/MildMod.htm">http://iccvam.niehs.nih.gov/methods/ocutox/MildMod.htm</a>

### ***In Vitro Test Methods for Detecting Nonsevere Ocular Irritants***

- Fluorescein Leakage Test Method
- Neutral Red Release Test Method
- Red Blood Cell Haemolysis Test Method

Ocular toxicity testing identifies substances that may cause irritation to the eye. Use of these <i>In Vitro</i> Test Methods will reduce and refine animal use for this purpose.		
Milestone	Date	Document Link or Relevant Webpage
ICCVAM Working Group Comment on Background Review Documents submitted the European Committee for the Validation of Alternative Methods	July 2008	-

### ***Non-animal Assessment Approach for Evaluating Eye Irritation Potential of Antimicrobial Cleaning Products***

Ocular toxicity testing identifies substances that may cause irritation to the eye. Use of this <i>in vitro</i> approach could replace animal use for this purpose to meet EPA labeling requirements.		
Milestone	Date	Document Link or Relevant Webpage
Submission by IIVS	January 2008	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/antimicro/SubmLtr-Stokes.pdf">http://iccvam.niehs.nih.gov/methods/ocutox/antimicro/SubmLtr-Stokes.pdf</a>
Peer Review Panel Meeting	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Peer Review Panel Report Published	July 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Recommendations Made to Federal Agencies	September 2010	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/AMCP.htm">http://iccvam.niehs.nih.gov/methods/ocutox/AMCP.htm</a>

### ***The In Vivo Low Volume Eye Test***

The low volume eye test is an alternative to the traditional <i>in vivo</i> rabbit eye test is also used as a reference method for <i>in vitro</i> methods under evaluation.		
Milestone	Date	Document Link or Relevant Webpage
Peer Review Panel Meeting	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Peer Review Panel Report Published	July 2009	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm">http://iccvam.niehs.nih.gov/methods/ocutox/PeerPanel09.htm</a>
Recommendations Made to Federal Agencies	September 2010	<a href="http://iccvam.niehs.nih.gov/methods/ocutox/AMCP.htm">http://iccvam.niehs.nih.gov/methods/ocutox/AMCP.htm</a>

### ***Immunotoxicity***

#### ***Murine Local Lymph Node Assay (LLNA)***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. Use of the LLNA reduces and refines animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Nomination by Sponsors	January 1998	-
Peer Review Panel Meeting	September 1998	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel98.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel98.htm</a>
Peer Review Panel Report	February 1999	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/llna/llnarep.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/llna/llnarep.pdf</a>
Recommendations Made to Federal Agencies	February 1999	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel98.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel98.htm</a>
Adoption of OECD Test Guideline 429	July 2006	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg429.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg429.pdf</a>
Update Submitted to OECD Test Guideline 429	July 2009	-
Update to OECD Test Guideline 429 adopted	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf</a>

#### ***Updated LLNA Test Method Protocol (20% animal reduction)***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. The ICCVAM-recommended revised protocol will <b>reduce</b> the number of animals used by 20% when the LLNA is used for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPrept2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPrept2008.pdf</a>
Update to OECD Test Guideline 429 Submitted	July 2009	-
Recommendations Made to Federal Agencies	September 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Recommendations to U.S. Federal Agencies Accepted	March 2010	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Update to OECD Test Guideline 429 Adopted	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf</a>

***Development of Performance Standards for the Murine Local Lymph Node Assay (LLNA)***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. Accepted performance standards will enable the development of new versions of the LLNA for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Draft Performance Standards Published	September 2007	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/llna/LLNAPerfStd12Sep07FD.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/llna/LLNAPerfStd12Sep07FD.pdf</a>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf</a>
Update to OECD Test Guideline 429 Submitted	July 2009	-
Recommendations Made to Federal Agencies	September 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Recommendations to U.S. Federal Agencies Accepted	March 2010	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Update to OECD Test Guideline 429 Adopted	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf</a>

***Reduced Murine Local Lymph Node Assay (rLLNA)***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. The reduced LLNA will reduce animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
CPSC Nomination	January 2007	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf">http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf</a>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf</a>
Update to OECD Test Guideline 429 Submitted (containing rLLNA procedure)	July 2009	-
Recommendations Made to Federal Agencies	Sept. 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Recommendations to U.S. Federal Agencies Accepted	March 2010	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PerfStds.htm</a>
Update to OECD Test Guideline 429 Adopted	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf</a>

***Nonradioactive Murine Local Lymph Node Assay (LLNA)***

- ***LLNA:DA***
- ***LLNA: BrdU detected by ELISA***
- ***LLNA: BrdU detected by flow cytometry***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. Nonradioactive version of the LLNA will refine and reduce animal use for this purpose by enabling more widespread use of the LLNA.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
CPSC Nomination	January 2007	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf">http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf</a>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel08.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel08.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf</a>
Revised Background Review Documents and ICCVAM Recommendations Published	March 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Second Peer Review Panel Meeting	April 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Second Peer Review Panel Report Published	June 2009	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2009.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2009.pdf</a>
ICCVAM Recommendations on Nonradioactive LLNA: DA and LLNA: BrdU-ELISA Methods Transmitted to U.S. Federal Agencies	June 2010	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna-NR.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna-NR.htm</a>
New OECD Test Guidelines for the LLNA: DA and LLNA: BrdU-ELISA Methods Adopted	July 2010	OECD TG 442A (DA): <a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG442A.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG442A.pdf</a> OECD TG 442B (ELISA): <a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG442B.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG442B.pdf</a>

***Use of the Murine Local Lymph Node Assay (LLNA) for Testing Pesticide Formulations, Metals, Substances in Aqueous Solutions, and Other Products***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. Use of the LLNA will refine and reduce animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
CPSC Nomination	January 2007	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf">http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf</a>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf</a>
Second Peer Review Panel Meeting	April 2009	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>

Second Peer Review Panel Report Published	June 2009	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2009.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2009.pdf</a>
ICCVAM Recommendations on the LLNA Applicability Domain Transmitted to U.S. Federal Agencies	June 2010	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna-app.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna-app.htm</a>
Update to OECD Test Guideline 429 Adopted	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG429-2010.pdf</a>

### ***Use of the Murine Local Lymph Node Assay (LLNA) for Skin Sensitization Potency Categorization***

Skin sensitization testing identifies substances that may act as sensitizers and cause the development of allergic contact dermatitis. Use of the LLNA will refine and reduce animal use for this purpose.		
Milestone	Date	Document Link or Relevant Webpage
CPSC Nomination	January 2007	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf">http://iccvam.niehs.nih.gov/methods/immunotox/llnadocs/CPSC_LLNA_nom.pdf</a>
Peer Review Panel Meeting	March 2008	<a href="http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm</a>
Peer Review Panel Report Published	May 2008	<a href="http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf">http://iccvam.niehs.nih.gov/docs/immunotox_docs/LLNAPRPRpt2008.pdf</a>
ICCVAM Recommendations Transmitted to U.S. Federal Agencies	Anticipated 2011	

### ***Dermal Phototoxicity***

#### ***Use of the In Vitro 3T3 NRU Phototoxicity Test***

<b>Dermal phototoxicity testing</b> identifies substances that may increase skin sensitivity to light so that they may be appropriately labeled and packaged. Use of the <i>in vitro</i> 3T3 NRU phototoxicity test will <b>refine and reduce</b> animal use for this purpose.		
Milestone	Date	Document Link or Relevant Webpage
OECD Test Guideline 432 Issued	April 2004	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg432.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg432.pdf</a>

### ***Dermal Absorption***

#### ***In Vitro Method for Measuring Skin Absorption***

<b>Dermal toxicity testing</b> identifies substances that may be poisonous when absorbed through the skin so that they may be appropriately labeled and packaged. Use of this test method may <b>reduce</b> animal use for this purpose.		
Milestone	Date	Document Link or Relevant Webpage
OECD Test Guideline 428 Issued	April 2004	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg428.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECDtg428.pdf</a>



### ***Genetic Toxicity***

#### ***Draft Test Guideline for the In Vitro Mammalian Cell Micronucleus Test***

Genetic toxicity testing identifies substances that may cause DNA damage and increase risk of cancer or birth defects. Use of the <i>In Vitro</i> Mammalian Cell Micronucleus Test could reduce animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Submission of ICCVAM Comments on Draft Test Guideline to U.S. OECD National Coordinator	February 2007	<a href="http://iccvam.niehs.nih.gov/methods/genetox/genetox.htm">http://iccvam.niehs.nih.gov/methods/genetox/genetox.htm</a>
Test Guideline 487 Adopted by OECD	July 2010	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG487.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/OECD/OECD-TG487.pdf</a>

### ***Developmental Toxicity***

#### ***Frog Embryo Teratogenesis Assay: Xenopus (FETAX)***

Developmental toxicity testing identifies substances that may cause birth defects so that they may be appropriately labeled. Use of FETAX could reduce or replace animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
EPA Nomination	May 1998	-
Background Review Document Published	March 2000	<a href="http://iccvam.niehs.nih.gov/methods/development/dev.htm">http://iccvam.niehs.nih.gov/methods/development/dev.htm</a>
Expert Panel Meeting	May 2000	<a href="http://iccvam.niehs.nih.gov/meetings/minutes/fetaxMin.pdf">http://iccvam.niehs.nih.gov/meetings/minutes/fetaxMin.pdf</a>

### ***Endocrine Disruptor***

#### ***Evaluation of In Vitro ER and AR Binding and TA Assays***

Endocrine disruptor testing identifies substances that may interfere with normal human and animal development. Use of <i>in vitro</i> tests could reduce animal use for this purpose in the EPA Endocrine Disruptor Screening Program (EDSP).		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
EPA Nomination	April 2000	-
Expert Panel Meeting	May 2002	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_EPrt.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_EPrt.htm</a>
Expert Panel Report	September 2002	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_EPrt.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_EPrt.htm</a>
Background Review Documents Published	October 2002	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_bckgnd.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_bckgnd.htm</a>
Test Method Evaluation Report Published	May 2003	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_TMER.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_TMER.htm</a>
Addendum to Test Method Evaluation Report Published	September 2006	<a href="http://iccvam.niehs.nih.gov/docs/endo_docs/EDAddendFinal.pdf">http://iccvam.niehs.nih.gov/docs/endo_docs/EDAddendFinal.pdf</a>

#### ***Xenobiotic Detection Systems, Inc. LUMICELL® ER Assay Validation Study***

Endocrine disruptor testing identifies substances that may interfere with normal human and animal development. Use of the LUMICELL® ER Assay could reduce animal use for this purpose in the EPA EDSP.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
LUMICELL® ER Assay Nomination	January 2004	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/ICCVAMSubmission28Jan05.pdf">http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/ICCVAMSubmission28Jan05.pdf</a>
Draft Pre-Screen Evaluation Released	August 2004	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/XDSeval2.pdf">http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/XDSeval2.pdf</a>
Submission of the Standard Project Submission Form to the OECD Test	September 2007	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/OECDdocs/LUMICELL/LUMICELL_SPSF.pdf">http://iccvam.niehs.nih.gov/methods/endocrine/OECDdocs/LUMICELL/LUMICELL_SPSF.pdf</a>

Guidelines Program: Stably Transfected Transcriptional Activation Assay for the Detection of Estrogen Receptor Agonists and Antagonists		
Validation Study Initiated	November 2007	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_eval.htm</a>
<i>Peer Review of Draft Background Review Document and Draft ICCVAM Test Method Recommendations</i>	<i>Anticipated 2011</i>	-

### ***CertiChem Inc. MCF-7 Cell Proliferation Assay Evaluation***

Endocrine disruptor testing identifies substances that may interfere with normal human and animal development. Use of the MCF-7 Cell Proliferation Assay could reduce animal use for this purpose in the EPA EDSP.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
MCF-7 Cell Proliferation Assay Nomination	June 2004	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/SubmDoc.pdf">http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/SubmDoc.pdf</a>
Pre-Screen Evaluation Released	October 2006	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/CCiPrescreenEval.pdf">http://iccvam.niehs.nih.gov/methods/endocrine/endodocs/CCiPrescreenEval.pdf</a>
Validation Study Initiated	June 2010	<a href="http://iccvam.niehs.nih.gov/methods/endocrine/end_eval-CCChem.htm">http://iccvam.niehs.nih.gov/methods/endocrine/end_eval-CCChem.htm</a>
<i>Peer Review of Draft Background Review Document and Draft ICCVAM Test Method Recommendations</i>	<i>Anticipated 2011</i>	-

### ***Pyrogenicity***

#### ***In Vitro Pyrogen Test Methods***

- The Human Whole Blood/IL-1 *In Vitro* Pyrogen Test
- The Human Whole Blood/ IL-1 *In Vitro* Pyrogen Test Using Cryopreserved Human Whole Blood
- The Human Whole Blood/IL-6 *In Vitro* Pyrogen Test (WB/IL-6)
- *In Vitro* Pyrogen Test Using Human Peripheral Blood Mononuclear Cells (PBMC/IL-6)
- An Alternative *In Vitro* Pyrogen Test Using the Human Monocytoid Cell Line MONO MAC 6 (MM6/IL-6)

Pyrogenicity testing is performed on products to be administered by injection to ensure that each lot of these products is free of substances that could induce a dangerous fever reaction. Use of these in vitro tests could replace animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Submission by ECVAM	June 2005	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyrodocs/supp/ecvampyro.pdf">http://iccvam.niehs.nih.gov/methods/pyrogen/pyrodocs/supp/ecvampyro.pdf</a>
Peer Review Panel Meeting	February 2007	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_PeerPanel.htm">http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_PeerPanel.htm</a>
Peer Review Panel Report Published	April 2007	<a href="http://iccvam.niehs.nih.gov/docs/pyrogen/PrRevPanFinRpt.pdf">http://iccvam.niehs.nih.gov/docs/pyrogen/PrRevPanFinRpt.pdf</a>
Final Background Review Document Published	October 2008	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_brd.htm">http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_brd.htm</a>
Test Method Evaluation Report Published	October 2008	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_tmer.htm">http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_tmer.htm</a>

Recommendations to Federal Agencies	November 2008	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm">http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm</a>
Acceptance of Test Methods by European Pharmacopeia	March 2009	
Acceptance by Federal Agencies	May 2009	<a href="http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm">http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm</a>

### ***Biologics and Vaccines***

#### ***Use of Humane Endpoints in Animal Testing of Biological Products and Rabies Vaccines***

Animal testing of biological products and rabies vaccines is performed to ensure that each lot of these products is safe and effective. A USDA directive refines animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
USDA Directive Published	April 2004	<a href="http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/USDA/CVB04-09.pdf">http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/USDA/CVB04-09.pdf</a>

#### ***Alternative Methods for Botulinum Toxin Potency Testing***

Animal testing of botulinum toxin is performed to ensure that each lot of this product is safe and effective. An ICCVAM-sponsored workshop explored ways to reduce, refine, or replace animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Nomination by the Humane Society of the United States	October 2005	<a href="http://iccvam.niehs.nih.gov/methods/biologics/botdocs/HSUSnomLD50.pdf">http://iccvam.niehs.nih.gov/methods/biologics/botdocs/HSUSnomLD50.pdf</a>
Workshop Held	November 2006	<a href="http://iccvam.niehs.nih.gov/methods/biologics/bot_workshop.htm">http://iccvam.niehs.nih.gov/methods/biologics/bot_workshop.htm</a>
Workshop Report Published	February 2008	<a href="http://iccvam.niehs.nih.gov/docs/biologics-docs/BoNTwkshprept.pdf">http://iccvam.niehs.nih.gov/docs/biologics-docs/BoNTwkshprept.pdf</a>

#### ***Alternative Methods for Animal Vaccine Potency and Safety Testing***

Animal testing of animal vaccines is performed to ensure that each lot of these products is safe and effective. An ICCVAM-sponsored workshop will explore ways to reduce, refine, or replace animal use for this purpose.		
<b>Milestone</b>	<b>Date</b>	<b>Document Link or Relevant Webpage</b>
Workshop Held	September 2010	<a href="http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm">http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp.htm</a>
<i>Workshop Report Published</i>	<i>April 2011</i>	-